A STUDY OF SECOND DEGREE BURN WOUND HEALING WITH TOPICAL HEPARIN COMPARED WITH TYPE I COLLAGEN

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CERTIFICATE

Certified that the dissertation entitled **"A STUDY OF SECOND DEGREE BURN WOUND HEALING WITH TOPICAL HEPARIN COMPARED WITH TYPE I COLLAGEN"** is a bonafide work done by **Dr. V. Dhamodara Raj,** Postgraduate, Department of Burns, Plastic and Reconstructive Surgery, Kilpauk Medical College, Chennai under my guidance and supervision in partial fulfillment of the regulation of the Tamil Nadu Dr. M.G.R. Medical University for the award of M.Ch (Plastic surgery) Branch-III during the academic period of August 2004 to August 2007.

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DECLARATION

I declare that the dissertation titled **"A STUDY OF SECOND DEGREE BURN WOUND HEALING WITH TOPICAL HEPARIN COMPARED WITH TYPE I COLLAGEN"** submitted by me for the degree of M.Ch Plastic Surgery is the record work carried out by me during the period of August 2004 to August 2007 under the guidance of Professor **Dr. A. DHANIKACHALAM, M.S., M.Ch, CTBS (USA),** Professor & Head of the Department, Department of Burns, Plastic & Reconstructive Surgery, Kilpauk Medical College, Chennai – 600 010 and as not formed basis of any Degree, Diploma, Associate ship, fellowship titles in this or any other University or other similar institution of higher learning

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CONTENTS

INTRODUCTION

Ever since man discovered fire, burns are among the oldest injuries man still suffers from. Since the days of Eber papyrus in ancient Egypt, the treatment of burns has advanced to the present day of skin substitutes. Autogenous skin remains the gold standard for burn would cover. But the paucity of available donor skin provided the impetus to look for materials that would provide temporary wound closure. During the recent past the use of biological and synthetic material in the temporary closure of the wound has become common place. During healing, the inflammatory phase is followed by the proliferative phase once the fibroblasts arrive and produce collagens, other proteins, glycosaminoglycans, the cells of tissue repair, and new capillaries in the granulation tissue.

Thus, during the granulation tissue formation two major extra-cellular matrix proteins – collagen and proteoglycans play an important role.

Though the efficacy of collagen and the heparin (a glycosaminoglycan) have been studied separately and found to be effective as against standard care with topical SSD, comparative study of burns treated with Heparin as a topical application and collagen have not been reported.

In our 50 bedded critical burn centre at the Govt. Kilpauk Medical College Hospital, Chennai, where about 7000 outpatients of burns are treated with about 1600 in patients annually, the need was felt to evaluate the efficacy of topical heparin as against Type I collagen sheets in the management of partial thicken burns as a temporary dressing modality.

AIM

To compare the outcome of partial thickness burns treated with topical heparin as against with collagen Type I to evaluate in each group the following.

1. Patient comfort with parameters like Pain, itching.

2. Healing time.

3. Length of stay in hospital.

4. The quality of the scar at the end of 6 months.

5. The cost benefit analysis.

REVIEW OF LITERATURE

Wound healing is a finely controlled biological process involving a series of complex cellular interactions. Following inflammation, the wound bed matrix is gradually replaced by granulation tissue followed by the long slow process where collagen accumulates and restores tensile strength. During healing, the inflammatory phase is followed by the proliferative phase once the fibroblasts arrive and produce collagen, other proteins, glycosaminoglycans, the cells of tissue repair, and new capillaries in the granulation tissue. Granulation tissue acts as a precursor to the formation of scar tissue. The role played by the extracellular matrix proteins from the initial days of healing, particularly during granulation tissue formation, is of great importance. Increasing evidence is available to show the necessity of appropriate extracellular matrix for morphogenesis, cell differentiation and in the maintenance of tissue – specific interactions. Along with these the cytokines have been implicated during the process of healing. During granulation tissue formation two major extracellular matrix proteins – collagen and proteoglycans play an important role. Collagen is involved from the very early stage to the final remodeled tissue formation. The many vital processes of fibroblast proliferation, matrix formation and remodeling during tissue repair depend on a precise timing and controlled balance in collagen synthesis and collagen turnover degradation.

The Anticoagulant effects of heparin and related molecules form the rationale for using heparin in the treatment of burns. Recent basic science literature suggests heparin may have a biological role as an anti-inflammatory, anti-angiogenic, and anti-metastatic agent. More importantly, at the molecular level, heparin may be an enhancer of wound healing, which has enormous implications for the treatment of acute and chronic burn wounds. In the immediate post-burn setting, the benefits of heparin's postulated anti-inflammatory and enhanced wound healing properties could include reduced pain (hence better compliance with dressing changes or physiotherapy), infection, length of hospital stay, and mortality. The long-term benefits of this expanded range of uses of heparin in the treatment of burn injury could include improved function and range of motion of extremities, reduced scarring, and possibly decreased psychiatric or psychosocial sequalae.

An expanded range of treatment options for burn injury is desirable given that 1.25 million people on average are treated annually for burns in the United States. Four percent of these people will require hospitalization and specialized burn care. Approximately 25 percent of people with severe burn injuries (greater than 75 percent of total body surface area) will die even after receiving advanced treatment at specialized burn centers. The morbidity from burn injury is also great. Short term morbidity

includes the pain of the injury and subsequent surgical therapy. Over the medium to long term, the psychosocial impact of disfigurement, and the potential for post-traumatic stress disorder, can have lasting ill effects on patients and patients' loved ones. The following question have to be looked into:

- **Does the method of application make a difference?**
- **Do the outcomes vary by the type or degree of burn?**
- **How do the outcomes of burn treatment with heparin compare to current treatment without heparin?**

Multiple roles for heparin in the treatment of burns were examined. These roles included wound healing and pain control, as well as the treatment of sepsis, inhalation injury, and venous thrombosis. However, there was insufficient data available to answer the key question. The research has been conducted in a multitude of different countries with varying standards of burn care. Thus, the available evidence was severely limited with respect to its relevance and applicability to current treatment standards in many locales. These deficiencies hampered the ability to judge the reported effectiveness of heparin in burn treatment

These contraindications of the use of Heparin in burns include bleeding diathesis, bleeding history, active bleeding or associated trauma with potential bleeding, active intestinal ulcer,

thrombocytopenia, liver disease, renal disorders, or allergy to heparin.

Saliba et al claimed that heparin had benefits for outcomes such as pain, cosmesis, and wound healing. Articles had problems regarding the use of invalid comparison groups or invalid outcomes. The major issue with comparison groups was the use of controls that were treated at earlier points in time, or at different hospitals, than people who received heparin. In both cases, different treatment protocols could have confounded the observed associations between treatment and outcome.

Regarding outcomes examined using a validated measurement instrument such as the McGill Pain Scale or other methods like quantity of analgesics required were employed to estimate the degree of pain relief in heparin versus control patients. For cosmesis, pictures were used to demonstrate the benefit associated with heparin use Confounding was not controlled in any of the abstracted articles. Furthermore, confounding could not be ruled out for the randomized controlled trials The evidence from the abstracted articles was not applicable to all clinical contexts. This was because the treatment protocols employed in the articles did not demonstrate a common standard of burn care. Reasons for the absence of commonality were temporal, i.e., the research was done before current standards were adopted, or contextual, i.e., the research was country specific and standards of

burn care differ between countries. If heparin is shown to promote wound healing of the donor area, then the next study would involve people (adults, adolescents, and children) with bilateral extremity burns to the arms, hands, or legs. People would serve as their own controls: topical heparin plus standard treatment would be applied to one extremity and standard treatment alone would be applied to the other extremity. Outcomes would be the same as in the first study, plus there would be an evaluation of quality of life.

All these studies would have to be organized at multiple sites to ensure that adequate numbers of patients are recruited to achieve high statistical power.

A general list of potential outcomes includes:

- Mortality
- Incidence of medical procedures following initial treatment with heparin or standard therapy (e.g., reintubation, excision, grafting)
- Functional performance (e.g., thumb opposition score, fingertip-to-palm distance, prehensile score)
- Pain (measured using the McGill Pain Scale)
- Scarring (measured using the Vancouver Scar Scale)
- Itching (measured via the amount of anti-pruritic medications used [e.g., Benadryl®])

- Quality of Life (measured using the Health Outcomes Burn Questionnaire for children and

Heparin

Heparin belongs to a family of polyanionic polysaccharides called glycosaminoglycans (GAGs). The structure of GAGs is described in terms of their prevalent repeating disaccharide sequences, which consist of alternating uronic acid and amino sugar residues. Heparin is a highly sulfated polysaccharide composed of hexuronic acid and D-glucosamine residues joined by glycosidic linkages. Heparin is a polydisperse compound with a molecular weight ranging from 3,000 to 30,000 Da (Daltons) (mean weight, approximately 15,000 Da). Commercial heparin, or unfractionated heparin (UFH), is isolated from mammalian tissues rich in mast cells. Heparin acts as an anticoagulant by activating antithrombin and accelerating the rate at which antithrombin inactivates clotting enzymes, particularly thrombin (factor IIa) and factor Xa. UFH also enhances the inhibition of factor IXa, factor XIa, and factor VIIa bound to tissue factor by antithrombin. Heparin binds to antithrombin through a high affinity pentasaccharide, which is present on about one-third of heparin molecules. Binding of heparin to antithrombin via its unique pentasaccharide sequence causes a conformational change in the reactive center loop of antithrombin that accelerates its interaction with factor Xa, but not with thrombin. For inhibition of thrombin, heparin must bind to both the coagulation enzyme and antithrombin. This bridging effect requires a heparin chain that contains at least 18 saccharides. By inactivating thrombin, heparin

not only prevents fibrin formation, but also inhibits thrombin-induced activation of platelets and factors V and VIII.

Besides binding to antithrombin, heparin also binds to a wide range of other proteins via electrostatic interactions. These proteins include heparin cofactor II, receptors, and growth factors. The relative strength of binding depends on the sulfation pattern, charge density, and molecular weight

Low Molecular Weight Heparins

During the last decade, low molecular weight heparins (LMWHs) have gradually replaced UFH for some clinical indications. LMWH is prepared from UFH by controlled enzymatic or chemical depolymerization. Like heparin, LMWHs are polydisperse and comprise heparin chains from 1,000 to 10,000 Da. The mean molecular weight of LMWHs is between 3,600 and 6,500 Da. About 15 to 20 percent of LMWH chains contain the antithrombin-binding pentasaccharide sequence. At least half of the pentsaccharide-containing chains of LMWH are too short to bridge thrombin to antithrombin. For this reason, LMWHs have reduced ability to inactivate thrombin. In contrast, the smaller molecular weight chains retain their ability to inactivate factor Xa because bridging between antithrombin and factor Xa is less critical. Compared to UFH, LMWHs exhibit a better subcutaneous bioavailability, a more predictable anticoagulant response, and a longer half-life.3 More

recently, synthetic analogs of the antithrombin-binding pentasaccharide sequence have been developed.

Non-Anticoagulant Effects of Heparin

Heparin possesses both a flexible structure and a high anionic charge that permits electrostatic interactions with a variety of different molecules. While heparin has been used largely for its anticoagulant effects, there is evidence that heparin and related molecules also possess anti-inflammatory and antiangiogenic properties, as well as a capacity for wound healing. These effects are discussed separately below.

Anti-Inflammatory Effects

Although the mechanisms responsible for the anticoagulant effects of heparin are well understood, the mechanisms underlying heparin's anti-inflammatory activity are not. The evidence that heparin possess anti-inflammatory properties comes mainly from cell culture and animal studies. The anti-inflammatory and immunomodulating effects are far-reaching and include influencing monocyte, T-cell and neutrophil activity, nitric oxide production, chemokine and cytokine activity, complement activity, platelet activation and aggregation, and smooth muscle cell proliferation.

Antiangiogenic and Antimetastatic Effects

There is increasing interest in a potential role for heparin and related molecules in the management of cancer patients. LMWHs have generated particular interest because they have been validated in both the treatment and prevention of thromboembolic disease in patients with malignancy. More interestingly, the benefits of LMWH therapy appear to be independent of any anticoagulant properties, which suggests that direct effects on tumor cell biology can help to explain the mechanism. Possible mechanisms include the inhibition of selectin-mediated cell-cell interactions, heparanase inhibition, binding of proangiogenic growth factors (e.g., basic fibroblast growth factor [bFGF] and vascular endothelial growth factor [VEGF]), and stimulation of tissue factor pathway inhibitor (TFPI) release.

Wound Healing Effects

A persistent inflammation with the accumulation of large numbers of neutrophils is characteristic of chronic wounds. Secretory products released from these cells, such as elastase, cathepsin G, and proteinases, are detrimental to wound healing because they degrade the extracellular matrix and growth factors and further recruit neutrophils to the wound area. Heparin and related molecules are thought to inhibit the action of these secretary products via electrostatic interactions.

Clinical Uses of Heparin

Since its discovery in 1917, heparin preparations have been used as an effective anticoagulant for thromboembolic prophylaxis and treatment. With over half a century of use, other roles for heparin have been elicited, including angiogenesis regulation, lipoprotein lipase modulation, maintenance of endothelial competence, and inhibition of vascular smooth muscle proliferation after injury. This section will focus on clinically proven and accepted applications of heparin. Heparin is the most widely used parenteral antithrombotic in clinical medicine due to its ease of administration and titration, availability, cost, known side-effect profile, and demonstrated clinical efficacy. Other parenteral antithrombotic agents available include heparinoids such as fondaparinux or direct thrombin inhibitors such as hirudin and bivalirudin. These drugs are more expensive, not as easily titrated and reversed, and have been studied in fewer clinical applications relative to heparin. Numerous guidelines define the role of heparin in thrombosis prevention and treatment; the American College of Chest Physicians (ACCP) guidelines are perhaps the most frequently cited.

Collagen and Burns

Collagen is the most common mammalian protein, an essential product of fibroblasts. Atleast 17 types of collagen have

been identified. The most known skin collagens are Type I, III, IV, V, VI and VII. Type I, III, and V are fibrillar type and are the normal components of dermis.

Fibrillar collagen type I and type III are the primary fibroplastic molecules associated with granulation tissue and scars. Type III is already forming with in 24 hours of burn injury, whereas Type I and its precursor molecule can be seen in 4 to 7 days. Type III fibrillar collagen is the first to be produced and most abundant. This is gradually reversed as the healing progresses and Type I becomes more dominant. Mature dermal tissue has a normal 1:3 collagen ratio of 4:1, however this normal proportion is never achieved by scar tissue.

Burn Injury

Approximately million people are treated annually for burn injuries in India. Four percent of these people require hospitalization and specialized burn care. High-risk populations for burn injuries include children, elderly, physically or mentally disabled.

Definition and Description of Burn Injury

Burn injuries are either partial thickness or full thickness in nature. Partial thickness burns involve the epidermis and various depths of the underlying dermis. These burns are diagnosed both

clinically and temporally. Partial thickness burns can be divided into superficial or deep Superficial partial thickness burns appear as an erythema (first degree) or blistering (second degree) on the skin. Very superficial burns correlate with injury to the epithelial layer of skin and usually heal without medical intervention or scarring (except for possible hyperpigmentation, which is usually temporary in nature [e.g., sunburn]). Superficial partial thickness burns heal within 7 to 14 days. A superficial partial thickness burn may also involve the superficial aspect of the dermis (second degree), which can result in blistering and scarring of the skin. The presence of varying shades of foci of pallor indicates deep partial thickness burns that heal within six weeks. However, healing may be incomplete. These burns scar the skin and frequently require grafting Surgical Full thickness burns result in injury and loss of the entire epithelium and dermis (third degree). A full thickness burn may also involve injury to underlying structures such as muscles, nerves, tendons, or bones (fourth degree). If left on their own, without surgical intervention, these burns would take well in excess of six weeks, or even months, to heal. These burns may cause significant scarring and, if present around joints, may severely limit the range of motion.

First degree - superficial (erythema) Second degree - deep (blister, pallor) Third degree - white, tan, beige, red, etc. skin color Fourth degree - involves tendon, bone, etc.

Burn injuries may also be classified according to the type of noxious agent causing the burn (e.g., flame, scald, flash, contact, smoke inhalation, electrical). Scald injuries, the most common burn injury in civilian populations, are secondary to contact with hot liquids. Hot water is the most common cause of scald injury, but other agents can include coffee, tea, soup, sauces, hot grease, or oil. Burns secondary to contact with tar and asphalt are also considered scald injuries.

Flame burns are secondary to contact with a source of open flame. House fires, careless smoking, automobile accidents, inappropriate use of flammable materials, and ignition of clothing are common factors associated with flame burn injury. Flame burns are associated with a serious and potentially fatal condition known as smoke inhalation injury. Inhalation injury is due to the exposure of the respiratory tract to steam and toxic inhalants from the smoke of a fire.

Flash burns are secondary to exposure to explosions of combustible or flammable materials. Contact burns are secondary to skin contact with hot items such as metal, glass, chemicals, plastic, or coals. Electrical burns are thermal injuries that occur when electrical energy is converted into heat upon contact with the skin. Electrical burns can severely affect deeper structures such as nerves or bones even when there is minimal damage to the overlying skin.

Burn Care

In the past three decades, burn care has undergone significant transformation, and this has led to markedly improved survivability. The health care system has developed a sophisticated approach to hospital burn care that is predicated on a network of specialized burn treatment centers. These centers are well equipped and professionally staffed to treat local injuries and to handle the transfer and treatment of serious burn injuries from more distant locales. This transformation of burn care reflects advancements in multiple areas of medicine, including critical care, wound infection control and antimicrobial therapy, surgical therapy (e.g., early excision and grafting), specialized burn care research, and coordinated methods of burn patient transfer (e.g., air ambulance and accompanying medical support services). Early excisional therapy of deep partial thickness or full thickness burns is common Burns that heal within three weeks commonly do well and are less likely to produce hypertrophic scarring or functional impairment. Burns that require more than three weeks to heal are commonly associated with hypertrophic scarring or functional impairment. For patients with small to moderate burn injuries where the healing time will exceed three weeks, early excision and

grafting is the recommended course of treatment. The benefits of early excision and grafting include decreased hospitalization, early return to work or school, enhanced functional status, and improved physical appearance. However, properly estimating the time to healing for a burn remains an important clinical challenge. Risk factors associated with mortality in burn injury include total body surface area (TBSA) greater than 40 percent, age over 60 years, and inhalation injury. Temporary or permanent disabilities are common in patients with significant burn injuries who are admitted to specialized burn care facilities. Reconstructive surgery and long-term rehabilitation are routine components of extended care for disabled burn patients.

Psychosocial Aspects of Burn Injury

The morbidity associated with burn injury is not limited to physical conditions such as pain or scarring. Psychiatric and psychosocial morbidities form important and often overlooked aspects of burn injury. Psychiatric and psychosocial morbidities are classified into pre- and post injury conditions. Pre-injury psychiatric conditions in adults may include depression, suicidality, substance abuse, and personality disorders. In children, pre-injury conditions may include behavioral disorders such as conduct disorder or attention deficit hyperactivity disorder.

In the post-injury phase, hospitalization and acute burn care can lead to psychiatric and psychosocial stresses for patients. Common psychiatric conditions include delirium, acute stress disorder (ASD), post-traumatic stress disorder (PTSD), and depression. Psychological suffering (i.e., PTSD) may also be manifest in the parents of children or adolescents with burn injury.

The first year post-burn injury may be particularly psychologically stressful for patients, but most adult and pediatric burn patients do not suffer long-term, burn-related, psychiatric sequelae. For a minority of burn injured patients, altered patterns of socialization may develop, especially for men with visible disfigurement. In women, decreased levels of sexual satisfaction are a frequent long-term result of burn injury.

*Outcomes***.** Studies with the following outcomes could be included:

1. Need for surgical procedure (e.g., grafting, debridement, fasciotomy, quality of graft take [percentage], re-grafting, reconstructive surgery);
2. Pain;
3. Transfusion rate;
4. Mortality (prior to, or after, discharge from hospital);
5. Length of stay in hospital;
6. Scarring (size, hypertrophic scarring);

7. Decrease in range of motion, function, or activities of daily living;
8. Respiratory measures (e.g., length of intubation);
9. Thrombosis and emboli;
10. Complications (e.g., bleeding, infection);
11. Rehabilitation;
12. Quality of life; and
13. Psychiatric adjustment (e.g., PTSD, anxiety, depression).

Three of the articles were randomized controlled trials (RCTs) in adult and pediatric burn patients. The first, by Srivastava et al., was a comparison of heparin and standard therapy to standard therapy alone. Heparin use was found to improve the following outcomes, mortality, infection rate, graft healing, and eschar separation. For mortality, three out of 25 people died in the heparin group, while 11 out of 25 people died in the control group. Infection rates were lower in the heparin group, with 20 people having wound infection versus all 25 people in the control group. Grafts healed 11 days faster on average in the heparin group and eschar separation was a mean of 9 days faster in the heparin group. The study had a clear monitoring protocol for adverse effects and no increases in bleeding were found as a result of heparin use. Lastly, the treatment regimen was a combination of systemic and topical heparins, so any potential therapeutic benefits

could not be attributed to one route of administration over the other.

Another RCT showed that topical heparin significantly reduced primary scarring in 37 heparin-treated adults and children. These people were compared to 27 controls who received standard therapy. However, the method of treatment allocation was not described in the publication and the outcome measures were not validated in burned patients. Thus, it is difficult to attribute the favorable outcome to heparin alone.

In a recent study by Venkatachalapathy et al., was conducted to examine the effect of topical heparin on clinical outcomes in people with second degree burns (age range:15 to 35 years). Control patients received usual treatment, which included topical antimicrobial cream, debridements, and skin graftings in the early post-burn period. Outcomes included length of hospital stay, mortality, and number of skin grafts. The authors found a significantly ($p<0.001$) shorter length of hospital stay in the heparin-treated patients (all 50 heparin-treated patients had lengths of stay about 40 days, while 28 of 50 control patients had stays of 40 to 50 days). There was also less mortality (0 heparin versus 5 controls) and fewer skin grafts (4 heparin versus 10 controls) in the heparin group. Two articles contained investigations of heparin's use in adult-only burn populations. The first, by Reyes et al., was a non-randomized, comparative (cohort)

study of nine patients who were injured in a thermal disaster. Four patients received topical heparin immediately after hospital admission and they were reported to have better pain relief, less swelling, fewer fasciectomies, a shorter length of hospital stay, and earlier burn revascularization than five control patients who did not receive topical heparin until 5 days after hospitalization.

While the results were positive for heparin, they must be interpreted. The other article about heparin use in adult burn patients was written by Acharya, who compared the effects of three therapies: 1) topical heparin, 2) topical heparin with topical steroid and antibiotic, and 3) topical steroid and antibiotic alone. The study showed no difference between treatment groups. Three studies focused on the use of heparin to treat burns in pediatric populations. Desai et al. conducted a non-randomized trial (cohort study) to examine the effect of aerosolized heparin with acetylcysteine for 7 days on inhalational burn injuries in children. The heparin/acetylcysteine group ($n = 47$) had significantly less reintubations, less atelectasis, and a lower mortality rate than the standard therapy group ($n = 43$, $p < 0.05$). A pediatric article was an unpublished cohort study to compare nine children undergoing standard burn therapy in 1998 to 10 children undergoing standard therapy plus heparin (intravenous followed by topical) in 1999. The authors measured pain using subjective, observational criteria like patient behavior (e.g., crying, struggling) and a decrease in the

"noisy din and distressing emotional ambience" of the hospital ward. These observations were not measured in a systematic, quantitative fashion and therefore should not be taken as indicative of a treatment effect.

Given the above review, some of the abstracted studies contain evidence that heparin has potential clinical benefits in the areas of reducing mortality, reducing pain, improving cosmesis, and alleviating lung injury in inhalational burns. However, these studies suffer from some limitations. In light of these limitations, the evidence supporting the use of heparin in burn injury cannot be considered strong and has to be investigated by RCTS.

There are insufficient data available to determine if the method of application of heparin in burn patients makes a difference with respect to clinical outcomes.

The following gaps exist within the literature. Four published studies and two unpublished manuscripts comparatively examined (e.g., treatment versus control) clinical outcomes in the use of heparin to treat burns. Another study had clinical outcomes, but the effect of heparin could not be separated from concomitant therapy. In these studies, no comparisons were made of systemic heparin (intravenous or subcutaneous) or topical heparin applications to the burn site.

There are insufficient data available to evaluate the outcome of treatment with heparin in Burns that vary by type of degree of Burn.

Outcomes of burn treatment with heparin compare to current treatment without heparin

Multiple roles for heparin in the treatment of burns were examined in the abstracted studies. These roles included wound healing and pain control, as well as the treatment of sepsis, inhalation injury, and venous thrombosis. However, there were insufficient data available to answer the key question. This was because the abstracted studies were conducted in eight different countries with varying standards of burn care and published over a time span of three decades. Thus, the studies simply did not encompass any standard, current burn treatment.

In addition, nine abstracted studies were primarily laboratory studies without clinical outcomes. Four of the abstracted articles specifically addressed the issue of contraindications to the use of heparin in burn patients. This was limited to listing contraindications for subcutaneous or intravenous applications of heparin such as bleeding diathesis, bleeding history, active bleeding or associated trauma with potential bleeding, active intestinal ulcer, thrombocytopenia, liver disease, renal disorders, or allergy to heparin. The authors of two articles wrote that these contraindications were exclusion criteria, while the authors of the other two articles wrote that none of the patients in their studies had any of these contraindications.

When using heparin in burn patients, it would be prudent to apply the same precautions as would be applied to the use of heparin in patients with thromboembolic disease. The most common contraindication for heparin in patients with thromboembolic disease is bleeding. The risk of bleeding increases with higher heparin doses and is associated with patients' anticoagulant responses, the method of heparin administration, the co-administration of anti-platelet or fibrinolytic agents, and recent trauma or surgery. Bleeding is as frequent with low molecular weight heparins (LMWHs) as with unfractionated heparin (UFH). In one study, bleeding was observed in 5.2 percent of patients who were given continuous intravenous heparin and in 4.1 percent of patients who were given subcutaneous heparin. Both groups received approximately the same mean dose over 24 hours.

Heparin can cause thrombocytopenia and is therefore contraindicated in patients who have had recent surgery (primarily for venous problems) or pre-existing cardiovascular disease primarily arterial). The incidence of thrombocytopenia was reported to be 0.3 percent in patients treated with heparin prophylaxis and 2.4 percent in patients treated with heparin therapeutically. Heparin-induced thrombocytopenia is an antibody-mediated process that can lead to arterial or venous thrombosis. The estimated incidence of vertebral fractures in people receiving long-term UFH therapy is three out of 100. Approximately 30 out of

100 people who receive therapeutic doses of heparin for longer than one month will experience reduced bone density that can lead to osteopenia or osteoporosis. The risk of osteoporosis was observed in groups of patients who had received long-term heparin therapy (> 6 months) at doses greater than 15,000 anti-Xa units. Much of the research on heparin and osteoporosis has been confined to pregnant women, so prolonged heparin use is contraindicated in this group. Osteoporosis is less common with LMWHs than with UFH.

Much of the available evidence regarding contraindications to heparin concerns subcutaneous or intravenous applications of the substance. In some of the abstracted articles, heparin was applied topically and there is no information regarding the contraindications of heparin when administered by this route.

Reported adverse effects of heparin in treating burns.

Srivastava et al. reported a clear monitoring protocol for adverse effects (in their case, bleeding) and they did not find any increases in bleeding secondary to heparin use. Two other articles contained reports of bleeding in heparin-treated patients. The incidence of bleeding was low when reported. One heparin-treated patient in a pediatric study (n = 19) bled on the burn surface. In another study (n = 9), three patients who received topical heparin beginning on the fifth day of hospital admission developed bleeding on day 8 of the study. However, the authors attribute the bleeding

to a treatment error: the dose of heparin was not reduced following burn revascularization. The bleeding may have been avoided if heparin was titrated properly.

HEPARIN TREATMENT REGIMENS AND RESULTS

Author	Type of Heparin	Method of Herparin Administration	Heparin Treatment Regimen	Outcomes	Results	Adverse Effects Heparin
Acharya	Hirudodi Anticoagulant (100 g) equivalent to 25,000 units of heparin)	Topical	NR	1) Pain relief (relief within 5 minutes to 3 hours) 2) Healed (Reductino of the burned or inflamed surface by ≥50% within 3 days)	1) Hirudoid cream group : 27/36 pain relief and 19/36 healed 2) Anacal ointment group : 16/16 pain relief and 4/16 healed 3) Antibiotic group : 24/33 pain relief and 16/33 healed	NR
Curreri et al.	NR	Subcutaneous	5,000 units	Fibrin split – product concentration	No quantitative data reported in the published article	NR
Desai et al.	NR	Aerosolized	5,000 units of aerosolized heparin alternating with 3 ml of a 20% solution of acetylcystine, every 2 hours for the first 7 days after injury	1) Reintubation 2) Atelactsis 3) Mortality	1) Reintubation : heparin group 3/47, control group 12/43 2) Atelactasis : heparin group 20/47, control group 30/43 3) Mortality : heparin group 2/47, control group 8/43	NR

Author	Type of Heparin	Method of Herparin Administration	Heparin Treatment Regimen	Outcomes	Results	Adverse Effects Heparin
lashvili et al.	NR	Subcutaneous	6,000 units in the 3 groups treated with heparin	1) Changes in the gastyrointestinal mucosa (e.g., ulcers, erosions, and hemorrhages) 2) Separation of the burn eschar 3) Time between burning and development of he wound surface ready for auto grafting 4) The period of treatment between burning and complete healing	1) Changes in the gastrointestinal mucosa : control group 12/20, group 4 (complete therapeutic regiment) 7/20 2) Separation of the burn eschar : 7-9 days faster in group 4 3) Time between burning and development of the wound surface ready for auto grafting : 44% shorter in group IV 4) The period of treatment between burning and complete healing : REduced 30 days in group 4	NR
Khadzhiiski et al.	Heparin (cream and dressing)	Topical	5,000 IU	Cicatrisation	Significant reduction in primary cicatrisation in 37 treated children and adults compared to 27 controls	NR

Author	Type of Heparin	Method of Herparin Administration	Heparin Treatment Regimen	Outcomes	Results	Adverse Effects Heparin
Kuz'muk et al.	NR	NR	NR	1) Prothrombin activity 2) Thrombotest value 3) plasma recalcification time 4) Plasma tolerance to heparin 5) Fibrinogen concentration	No quantitative data reported in the published article	NR
Loebl et al.	NR	Subcutaneous	20,000 units in four divided doses	Autologous half-life of erythrocytes	No quantitative data reported in the published article	NR
Mariano et al.	NR	Continous infusion	Heparin + CPFA as renal replacement therapy	1) Blood flow 2) Used Cartridges/session 3) Blood iCa 4) Blood pH and bicarbonates	No quantitative data reported in the published article	NR
Mims et al.	Beef lung and intestinal mucosal	NR	Heparin not used for treatment (heparin was used as a reagent)	Platelet aggregation	In contrast to controls, 15% of blood samples from burn patients demonstrated spontaneous aggregation, and 69% showed either first or second phase	NR

Author	Type of Heparin	Method of Herparin Administration	Heparin Treatment Regimen	Outcomes	Results	Adverse Effects Heparin
					aggregation after exposure to heparin	
Ono et al.	NR	Infusion	10,000 – 20,000 IU daily	1) Platelet counts 2) Finrinogen levels 3) Plasminogen levels 4) Fibrin degradation product levels	No quantitative data reported in the published article	NR
Peng et al.	Heparin and low molecular weight heparin	Intravenous	100 – 1,500 units	1) Median stay in ICU 2) Total days in hospital 3) Mortality	No quantitative data reported in the published articles	No heparin – related adverse effects observed
Reyes et al. 2001	NR	Infusion, subcutanesou, sprayed or dripped via needle, aerosolized	1st applicaiton was 5,000 IU/ml dripped or sprayed on open burn surfaces or injected into burn blisters – retreatment at 5 – 10 minute intervals for 20 – 30 minutes	1) Mean doses of pain medication 2) Swelling 3) Fasciectomy 4) Burn revascularization	1) Mean doses of pain medicaiton: heparin group (received heparin day 1) = 4 doses, control group (received heparin day and 5 and later) = 24 doses 2) Patients given heparin on day 1 had less burn swelling and body swelling, and no fasciectomies, compared to patients given heparin on day	Bleeding

Author	Type of Heparin	Method of Herparin Administration	Heparin Treatment Regimen	Outcomes	Results	Adverse Effects Heparin
					5 3) Burn revasularization was faster in patients given heparin on day 1	
Srivastava et al.	NR	Topical and systemic	1) Systemic route : 10,000 units 10% burn area, repeated every 4-6 hours; increased to maximum 300 – 400 units / 15% burn / kilogram body weight 2) Topical application ; 25,000 units / 10% burn	1) Mortality 2) Mean healing time 3) Full thickness Eschar separation 4) Raw area fit for grafting 5) Graft take	1) mortality : heparin group 3/25, control group 11/15 2) Mean healing time : heparin group 6 days (superficial) and 15 days (deep dermal), control group 10 days (superficial) and 28 days (deep dermal) 3) Eschar separation : heparin group 20 days, control group 36 days 5) Graft take : heparin group 95% control group 65%	No observed bleeding
Venkata-tachala – pathy et al.	Heparin sodium solution (boving	Dripped onto buirn surfaces or injected into burn blisters	200 IU/ml	1) Mortality 2) Days in hospital 3) Number of skin grafts	1) Mortality : heparin group 0/50, control group 5/50 2) Days in hospital :	NR

Author	Type of Heparin	Method of Herparin Administration	Heparin Treatment Regimen	Outcomes	Results	Adverse Effects Heparin
	intesinal mucosa)				heparin group had 29 patients discharged in ≤ 10 days, control group had 3 patients discharged in ≤ 10 days 3) Number of skin grafts : heparin group 4/50, control group 10/50	
Wahl et al . (a) (b)	Low molecular weight heparin (enoxaparin)	Subcutaneous	40 units 4x/day	Development of upper or lower extermity DVT or pulmonary embolism	7 patients had DVT (1 patient had upper extermity DVT and 2 patients had both upper and lower extermity DVT). 6 patient had superficial vein thrombosis (SVT) in the upper extremities.	NR

Study outcomes: A variety of clinical outcomes should be considered for the next generation of studies on heparin and burns. The outcomes would vary slightly depending on whether adult or pediatric populations are studied. Some of these outcomes are:

1. Mortality
2. Incidence of medical procedures following initial treatment with heparin or standard therapy (e.g., reintubation, excision, grafting);
3. Pain (measured using the McGill Pain Scale)
4. Scarring (measured using the Vancouver Scar Scale)
5. Itching (measured via the amount of anti-pruritic medications used [e.g., Pedichloryl®])
6. Quality of Life (measured using the Health Outcomes Burn Questionnaire for children and the Burn-Specific Health Scale100 for adults); and
7. Post-traumatic Stress Disorder (measured using the Child Stress Disorders Checklist101 for children and a selected range of measurement methodologies for adults).

Studies that are designed with the above precepts in mind will overcome the pitfalls of the abstracted articles and provide the clinical community with a clearer picture of the efficacy of the various uses of heparin in the treatment of burns.

MATERIAL AND METHODS

Place of study

The study was done at Department of Burns and Plastic surgery, Govt. Kilpauk Medical College, Chennai – 600 010.

Duration of Study

In the period between Jan 2005 to Jan 2006. Forty patients, with adults and children with second degree burns and scalds with TBSA burn 7% to 25% were recruited at random. They were allotted in to 3 separate treatment groups. Group A patients numbering 10 were treated with topical heparin in addition to the standard protocol burns management. The group B patients numbering 10 were treated with Healicoll™ (a Type I Collagen sheet preparation).

Group C had 10 patients with symmetrical burns on either side who served as their own control with Heparin on one side and Collagen applied on other side.Thus making 20 burn wounds treatment with heparin and the other 20 burn wound treated with Type1 collagen.

Inclusion Criteria

1. TBSA burns size from 5% to 25%.

2. Partial Thickness (second degree) Burns.

3. Age from 1 year to 60 years.

4. Flame burns, scalds, steam burns were included.

Exclusion Criteria

1. Burns with TBSA more than 25%.

2. Patients aged more than 60 or less than 1 year .

3. Electric Burn.

4. I degree and full thickness burns.

General treatment of Group A & Group B

All the 40 patients enrolled were initially assessed at arrival for the estimation of TBSA size. For calculating the TBSA, the Lund and Browder chart was used. The degree of the burns was assessed clinically. Rapid physical examination of vital signs, mental status, adequacy of lung air entry were done.

The superficial second degree burn were diagnosed based on clinical ground by the presence of

1. Red Appearance

2. Blisters

3. Blanching on finger pressure.

4. Intact tactile & pressure sensation

The second degree deep burns were recognized by the dry, mottled wound appearance and failure to blanch under digital pressure. All the patients had immediate intravenous lines secured with 18G large bore canula. Emergency sedation with Pedichloyl for paediatric patient and with Inj. Pentazocine with Promethazine was administered to adult. Prophylactic tetanus toxoid was routinely administered. Systemic antibiotics was given to all the patients according to the antibiotic policy of the department, which consisted rotation of empirically administered antibiotics based on the monthly antibiogram audit report of the preceding month, which included either single or combination of Ampicillin, Gentamycin, Amikacin, Cefotaxime, Cerftriaxone and Metrogyl in the standard dosages. These patients were neither catheterized nor had Ryles tube insertion. Emergency base line investigation for estimation of haemoglobin, hematocrit, RFT, and electrolytes were done wound swab was not done on the day of admission.

Modified Parkland formula (3 x TBSA x wt in kg) was used to calculate the IV fluid requirement for both adult and paediatric subset with 10% TBSA burn on more.

To avoid any confounding effect due to intravenous heparin on the outcome, both the group A & B & C were not administered intravenous heparin, which otherwise is the standard protocol followed in the department.

Local treatment of Group A

Under mild sedation, the local debridement of the wound was done routinely in bed side. The blisters were routinely removed by mechanical cleaning of skin. The wound washed with 5% povidone iodine with saline. Heparin sodium IP in the concentration of 5000 IU/ml was sprayed over the cleaned wound with 10cc syringe and 25G needle. The topical heparin dose was calculated with the formula 5000 IU x TBSA / day. Half of the calculated dose was sprayed over the wound and the remaining was diluted with saline and gauze pieces soaked in this heparin saline were used to cover the burn wound. Surgical pads were not used and heparin saline gauze dressing covered with bandages. The dressing was changed the next day and same amount of heparin was used till wound epithelialised.

Local treatment of Group B

Under mild sedation, the local debridement of the wound was done routinely bedside. The blisters were removed. Mechanical cleaning of skin done in the same way, wound cleared with 5% povidone and saline. A collagen based sterile wound dressing Healicoll™ (containing sterile reconstituted Type I collagen sheet, a semi-occlusive and would adhesive dressing (Advanced biotech production (P) Ltd., India) was applied to the wound. The collages sheet was put in saline for a few seconds for easy application and

was not necessarily rinsed thoroughly as it did not contain any irritant preservatives. The spread collagen sheets were allowed to dry in room air and temperature for few hours till wound adherence was complete.

Local treatment of Group C

These patients selected when they had symmetric distribution of burns on either side of the body so that they served as their own control on one side treated with Heparin and the other side treated with Type I Collagen sheet (Healicoll ™)

Measurement of outcome

Complete epithelialisation was certified by a senior faculty. The patients with Healicoll group B were discharged in a day and were asked to come for review and alternate days to the OPD. Group A patients on Heparin topical therapy were usually treated as inpatients till complete epithelialisaiton since they needed daily dressing.

(1) Healing time

Complete epithelialisation was certified by either the chief of the department or a senior faculty and the same was noted.

(2) Patient comfort

(a) Pain : The pain was subjectively recorded as stated by the patients in a visual analog pain scale of 1 – 10. The pain scale reading was taken on the day 2 and day 4 and the average was recorded.

(b) Itching : The itching was graded into mild moderate or severe and the subjective description of the patient was recorded at the time of complete would epithelialisation.

(3) Length of stay in hospital and mortality rates were recorded from case records.

(4) Scar assessment

The patients scar was assessed at the time of complete epithelialisation and at 2 months. The patients were communicated by post at the end of 6 months to report to the burns unit for scar assessment.

The scar assessment was objectively recorded using he Vancouver scar scale.

Vancouver Scar Scale

I Pigmentation

grade 0 (Normal colour)

grade 1 (Hypopigmentation)

grade 2 (Hyperpigmentation)

II Scar Thickness

grade 0 (Normal)

grade1 (less than 2 mm)

grade2 (2 to 5 mm)

grade3 (more than 5 mm)

III Itching

Grade1 (mild)

Grade2 (moderate)

Grade3 (severe)

IV Scar texture

grade 0 (Normal)

grade1 (supple)

grade2 (yielding)

grade3 (firm)

grade4 (banding but no limitation of ROM)

grade5 (Contracture)

To avoid observer variation, the scar assessment with the above criteria were done by same observer and recorded in the proforma. The observer was in unaware of the primary treatment modality of the burn wound to avoid bias.

RESULTS

I AGE

Children	Adults
19	11

Superficial second degree burns for the study were contributed by 66% paediatric patients defined as age below 12 years.

II PERCENTAGE OF BURNS

TBSA	Children	Adult
Upto 8%	8	2
9 – 16%	7	4
17 – 25%	4	5

Of the above patients wherever the patient had symmetrical distribution on either side, the patients formed their own control group by application of heparin on one side and Type II Collagen Healicol on the other side. (n = 10).

III CAUSE OF BURNS

	Scalds	Flame burn
Children	16	3
Adults	6	5

Majority of the study group consisted of accidental scalds in children (72% were scalds).

IV TIME TAKEN FOR EPITHELIALISATION

	Heparin	**Collagen**
7 – 8 days	1	-
9 – 10 days	10	6
11 – 12 days	5	9
13 – 14 days	3	5
15 – 16 days	-	-
17 – 18 days	1	-

It was noticed that heparin group epithelialised faster as the collagen group took more time to get separated. Two patients on topical heparin who developed mild wound infection took more time to heal.

V PAIN, COMPLICATIONS AND MORTALITY

	Heparin	**Collagen**
Wound infection	2	-
Bleeding	-	-
Sensitivity reactions	-	-
Mortality	0	0
Pain estimate by analog visual scale	**3.2**	**4.8**

No case of bleeding was noted with 5000 IU/ml concentration of topical heparin. Type I collagen sheet remarkably had no infective complications. Heparin group patients were more cooperative for mobilisation due to less pain as against the collagen group who experienced pain and stiffness due to collagen drying up.

VI ITCHING ON COMPLETE EPITHELIALISATION

	Heparin	Collagen
Mild	-	3
Moderate	-	1
Severe	-	-

Collagen group needed mild doses of chlorpheniramine maleate to alleviate mild pruritus. About 20% of collagen applicated wounds experienced mild itching at some point of time.

VII SCAR COLOUR ASSESSMENT AT 2 MONTHS

Color of the Scar	Heparin	Collagen
Grade 0	2	0
Grade 1 (pink)	16	10
Grade 2 (Red)	2	9
Grade 3 (Purple)	0	1

Pink colour represented good scar. Red and purple scars were adviced compression garments to avoid Hypertrophic scar.

VIII REQUIREMENT OF OTHER SURGICAL PROCEDURES

Only superficial second degree burns were consciously selected for the study. In both group complete epithelialisation was observed sooner or later and none in the study group needed grafting nor any other surgical procedures like escharatomy.

IX VANCOUVER SCAR SCALE ASSESSMENT AT 6 MONTHS

Pigmentation	Heparin	Collagen
Grade 0 near normal	11	1
Grade 1 (Hypo pigmentation)	9	18
Grade 2 (Hyper pigmentation)	-	1

Collagen group healed with significant hypopigmentation (59%), though not complained by the patients themselves.

B

Scar Thickness	Heparin	Collagen
Grade 0	16	8
Grade 1 < 2mm	3	8
Grade 2 - 2 – 5mm	1	3
Grade 3 > 5mm	0	1

63% applications of heparin healed with good scar thickness defined as grade 0 or grade 1 as against 52.8% good scar thickness in Type I collagen.

Scar Texture	Heparin	Collagen
Grade 0	9	5
Grade 1 supple	9	8
Grade 2 yielding	2	3
Grade 3 firm	-	4
Grade 4 Binding / Blanching	-	-
Grade 5 contracture	-	-

Clinical palpation methods showed smoother and supple scars with heparin group. Palpable roughness was noticed in the collagen group healing, though no overt banding nor contractures in either group.

D ITCHING AT 6 MONTHS

	Heparin	Collagen
Grade 0	20	17
Grade 1	-	3
Grade 2	-	-
Grade 3	-	-

9% of the wounds in collagen group had mild itching at 6 months which required seasonal medication. No itching noted with heparin.

X SCAR ASSESSMENT BY THE PATIENT / OR / RELATIVES

	Heparin	**Collagen**
Good	18	17
Satisfactory	2	3
Poor	-	-

Though there were perceptible minor differences in scar, suppleness, texture and pigmentation, the patients, themselves were happy about the outcome with 90% of heparin group and 88% of collagen group reporting their scar as 'good'.

DISCUSSION

Though both collagen as biological dressing and topical heparin have been validated in the management of partial thickness burns, no randomized control study have been done to evaluate the supremacy one over the other. Comparisons have been done with subjects taken during deficit times and of different age groups with similar burns. However, the assessment of partial thickness burn as superficial or deep is mostly by clinical methods and are open to observer variation.

In this study topical heparin is used as once a day application as partly as spray and partly as heparin impregnated gauze dressing, after debriding the burn blisters. Saliba et al and few other burn centers have used heparin in the concentration of 5000 IU/ml. In a study by Mohankumar et al from Pondicherry, Heparin was used in the concentration of 200 IU/ml by adding 20.8 ml of Heparin to 500ml of NS and same sued as a continuous drip irrigation. The investigation have not debrided burn blisters but have irrigated the blisters and allowed the blister skin to remain as a desiring.

This study had more of scalds (73%) and 63% of the subject were of pediatric age group. It was noted that 80% of pediatric burn were due to accidental scalds.

On topical spraying of heparin sodium IP in the concentration of 5000 IU/ml, at an average dosage of 5000 units per percent of burnt area (1ml per 1% burn) the patients experienced a mild burning sensation for 2 – 3 seconds which was followed by immediate pain relief. The paediatric age group patients could get rid of the apprehension are they could experience the pain relief.

For smaller area of burn less than 10% TBSA, though the hospital policy is to treat on outpatient basis, the patients of the heparin study group had to be admitted to make convenient the daily dressing charges. Whereas the collagen group of patients were routinely discharged after few hours after the collagen dried up or the next day.

2 Cases of minor wound infection was noticed in the heparin group as against no such infection in collage group. This is understandable due to the large load of burn patients with varying septic load being managed in the common ward and considering the non occlusive nature of during with topical heparin. The infection in the 2 cases leads to delayed wound epithelialisation in them by 5 days.

In the 10 patients in group C who was treated with either form of dressing on either half served as their own controls. It was well noticed that the ability and ease of functional mobilisation and joint stretching manouvers by the physiotherapy team was easier

and had good patient co operation in the sides where heparin was used. The collagen on drying up created a feeling of 'catching up the skin' on attempted mobilisation and co operation for functional mobilisation with collage was visibly less.

The change of dressing daily with the topical heparin was a substantial discomfort to the patient on the heparin soaked gauze drying up and stuck to wound and was painful while changing. The daily dressing was an ordeal for the patient as it is not possible in a large burn care centre as ours to give adequate sedation for daily dressing changes and the time to be allotted to the patient for daily dressing change by the surgeon was more. These two factors are a definite disadvantage with topical heparin therapy.

The collagen stuck to the wound and even after epithelialisation some fragments were skill stuck to the healed wound and gave the impression of more time for epithelialisation.

A Substantial percentage of 20% with collagen experienced pruritus at time of complete wound healing and for months after complete wound healing. The reconstituted collagen might have caused more aggregative of mast cells causing itching. But the itching persisted for months and the reason for the prolonged sensation of itching has to be studied further and remedied.

The Vancouver scar scale was specifically introduced for the burn wound in 1991.

The parameters like color and pigmentation are observer dependent and hence they were done by the same observer who was a senior faculty member of the centre. The more recent methods of scar assessment by volumetry or ultrasanography are not available and not practical. The thickness of the scar was measured by clinical means by palpation and no special techniques like photothesiometry were used.

The scar outcome at 2 months and again at 6 months were favourable with the heparin group, with no itching attack. There were small difference in the texture of the collagen group and heparin group. Though they were of academic importance the patient was happy with the outcome on either group and they rated than scar outcome as good. Most of the patients were not worried about minor pigmentary variations of the healed skin, even when in exposed parts of the body.

In superficial second degree burns (mostly scalds)the collagen application notably had left a healed wound with marked hypopigmentation at 6 months. The behaviour of this healed ulcer beyond 6 months needs to be studied further.

The cost of dressing material needed for a 5 percent burn wound in an average adult with Healicoll Type 1 collagen sheet worked to Rs.1800. The cost of Heparin for treating similar percent burns worked to Rs.450. But this may be an over simplification as

the repeated dressing time, the saline, the dressing gauze material and technical man hours , the significant hospital stay with heparin treatment are all to be taken in to account and thse parameters can not be quantified. But it was commonly noticed during the study that patients and their attenders wished to get out of hospital sooner but had to be retained for the sake of daily dressings, whereas the collagen group patients were discharged in a day or 2 . Hence the cost of the total treatment can not be confused with the cost of dressing material only. The hidden costs and discomforts are far greater with the heparin treatment group.

CONCLUSION

1. Topical Heparin in concentration of 5000 IU/ml per percent TBSA burns per day is safe and has no bleeding complications and needs no monitoring by BT, CT or PTT.
2. The final scar outcome with parameters such as scar itchiness, texture and pigmentation are favourable with topical heparin therapy. However the patient's satisfaction level are same for both groups.
3. The wound infection rate is less with collagen sheet dressing when compared to topical heparin.
4. Hospitalization and patient discomfort, technical labour required are all significantly high with topical heparin.

May be concluded that Type I collagen sheet dressing is preferable to heparin dressing in a large burn centre such as KMC in view of faster patient turnover, lower infection rate, ease of management and single application time, significantly reduced hospital stay and comparable patient satisfaction level of final scar outcome.

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PROFORMA

Burn wound healing heparin vs collagen

1. Name Age : Sex :

2. Address : IP No. :

DOA :

DOD :

3. TBSA % Burn

4. Occupation

5. Time of Accident Time of reporting for treatment

Date : Time : Date : Time :

6. Type of wound

Burn Scald

7. Wound care ☐ Collagen Type I

☐ Heparin

8. Hospital stay duration

9. Pain score on visual scale of 1 – 10

Day 2	
Day 4	
Average	

10. Time for epithelialisation

7 – 8 days

8 – 9 days

9 – 10 days

11. Itching severity on epithelialisation

Nil	Mild	Moderate	Severe

12. Compliance for physiotherapy / mobilisation

Poor	Satisfactory	Good

13. Sear outcome at 6 months (Vancouver scar scale)

A) Pigmentation

0	1	2

B) Texture

0	1	2	3	4	5

C) Thickness

0	1	2	3

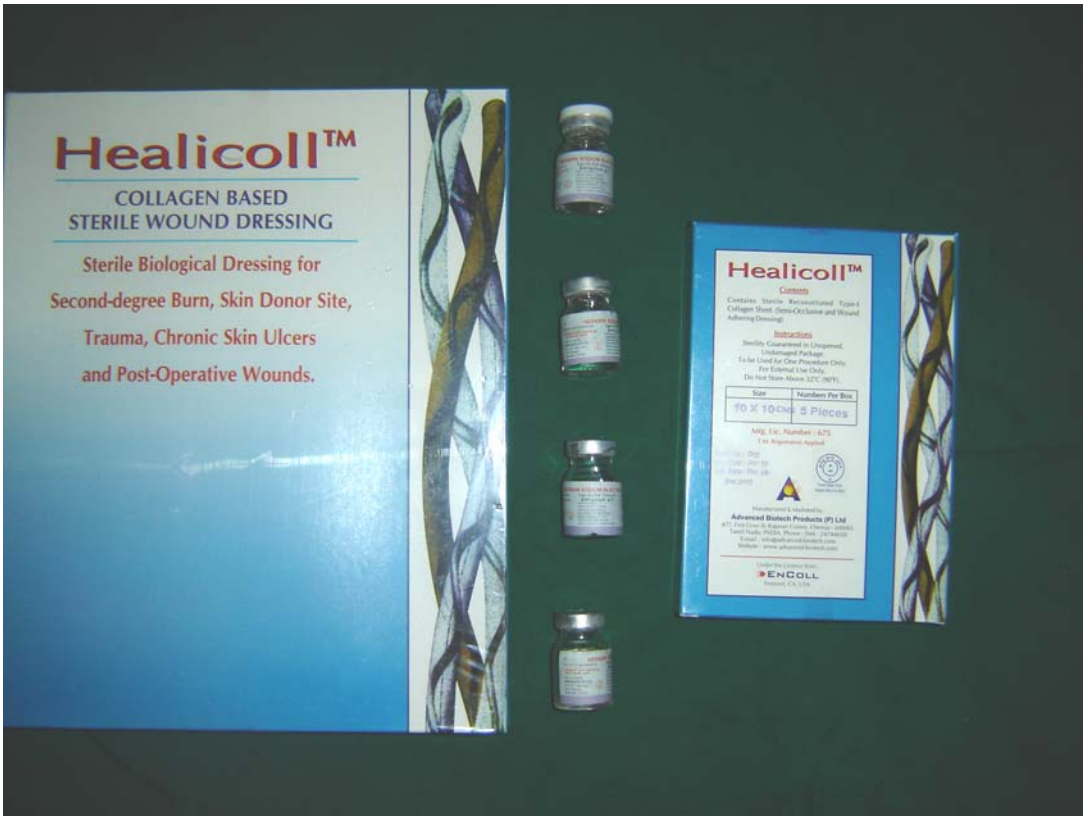
D) Itchiness

0	1	2

14. Complication of treatment

15. Cost of treatment

Dry type I Collagen Healicoll™ and Heparin Sodium IP



How the wound responds immediate post burn differentially

→ **DAY 1**

DAY 3 →

→ **DAY 5**

DAY 8 →

Patient as his own control Collagen Vs Heparin

Comparative healing in Face

Collagen **Heparin**

Collagen **Heparin**

Hypopigmentation observed with Healcoll at 6 months

Comparative Healing Trunk

Heparin **Collagen**

Comparative Healing Forearm

Comparative Healing Forearm

Collagen

Heparin